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10/804,954	03/19/2004	Marise S. Gottlieb		8077

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ROBERT E. BUSHNELL & LAW FIRM
2029 K STREET NW
SUITE 600
WASHINGTON, DC 20006-1004

EXAMINER	
CORDERO GARCIA, MARCELA M	
ART UNIT	**PAPER NUMBER**
1654	
MAIL DATE	**DELIVERY MODE**
05/28/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/804,954	GOTTLIEB, MARISE S.	
	Examiner	Art Unit	
	MARCELA M. CORDERO GARCIA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-9,11 and 13-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6-9, 11, 13-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-4, 6-9, 11, 13-17 are pending in the application. Applicant has amended claims 7, 11, 13, 14 and 17.

Claims 1-4, 6-9, 11, 13-17 are presented for examination on the merits.

Any previous rejection, which is not further restated herein, is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 6-9, 11, 13-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims are drawn to several methods of treatment comprising Purified Leukocyte Dialysate Subfraction. With regards to the term “Purified Leukocyte Dialysate Subfraction”, the disclosure provides the following guidance: “The "selected immunoregulators" ("selected immunormodulators" "selected immunoamplifiers") include the purified Leukocyte Dialysate Subfraction (LDS) described by Dr. A. Arthur Gottlieb Patents (U.S. Pat. Nos. 5,100,663, 4,616,079, 4,699,898, 4,710,380, 4,778,750, 4,874,608, 5,013,546, 5,081,108, 5,093,321 which are incorporated herein by references) which is naturally derived from healthy human leukocytes, as well as purified immunologically active

components of the naturally derived immunoregulators including the dipeptide tyrosylglycine (YG) and the tripeptide tyrosylglycylglycine (YGG), as well as synthetically produced YG and YGG. These regulators also include covalently modified YG and YGG, such modifications designed to stabilize or to enhance the biological activity of said regulators, as well as pharmaceutically acceptable salts, suitable for human use, of YG, YGG, and related molecules including covalently modified YG, and covalently modified YGG. " ([0041])." However, the disclosure and patents do not clearly set forth what is a subfraction and the term "Purified Leukocyte Dialysate Subfractions" is not defined expressly in any of the patents. Since this term is not expressly defined in any of the previous related patents nor is it expressly defined in the instant disclosure, there is no evidence of possession of the full scope of the claimed subfractions. It would therefore require undue experimentation as applicant has not shown possession nor adequate guidance to obtain the full scope of purified leukocyte dialysate subfractions having the therapeutic activities as instantly claimed.

Applicant's arguments

The examiner's rejection is not proper.

The examiner did not consider the references which are incorporated in the specification by reference. In the definition section of the instant specification, the purified Leukocyte Dialysate Subfraction was described as follows:

"[0041] The "selected immunoregulators" ("selected immunomodulators" "selected immunoamplifiers") include the purified Leukocyte Dialysate Subfraction

(LDS) described by Dr. A. Arthur Gottlieb Patents (U.S. Pat. Nos. 5,100,663, 4,616,079, 4,699,898, 4,710,380, 4,778,750, 4,874,608, 5,013,546, 5,081,108, 5,093,321 which are incorporated herein by references) which is naturally derived from healthy human leukocytes, as well as purified immunologically active components of the naturally derived immunoregulators including the dipeptide tyrosylglycine (YG) and the tripeptide tyrosylglycylglycine (YGG), as well as synthetically produced YG and YGG. These regulators also include covalently modified YG and YGG, such modifications designed to stabilize or to enhance the biological activity of said regulators, as well as pharmaceutically acceptable salts, suitable for human use, of YG, YGG, and related molecules including covalently modified YG, and covalently modified YGG."

The examiner did not consider the prior art references which are incorporated in the specification by reference, and did merely argue that the subfraction encompassed a myriad of subfractions. Please note that all the U.S. Pat. Nos. 5,100,663, 4,616,079, 4,699,898, 4,710,380, 4,778,750, 4,874,608, 5,013,546, 5,081,108, 5,093,321 are incorporated in the specification by references. Please note that the information incorporated is as much a part of the application as filed as if the text was repeated in the application. See below MPEP section. MPEP §2163.07(b) states that:

"Instead of repeating some information contained in another document, an application may attempt to incorporate the content of another document or part thereof by reference to the document in the text of the specification. The information incorporated is as much a part of the application as filed as if the text was repeated in the application, and should be treated as part of the text of the application as filed.

Replacing the identified material incorporated by reference with the actual text is not new matter. See >37 CFR 1.57 and MPEP § 608.01(p) for Office policy regarding incorporation by reference. See MPEP § 2181 for the impact of incorporation by reference on the determination of whether applicant has complied with the requirements of 35 U.S.C. 112, second paragraph when 35 U.S.C. 112, sixth paragraph is invoked."

Therefore, when considering U.S. Pat. Nos. 5,100,663, 4,616,079, 4,699,898, 4,710,380, 4,778,750, 4,874,608, 5,013,546, 5,081,108, 5,093,321, and it is further defined as being "naturally derived from healthy human leukocytes, as well as purified immunologically active components of the naturally derived immunoregulators including the dipeptide tyrosylglycine (YG) and the tripeptide tyrosylglycylglycine (YGG), as well as synthetically produced YG and YGG", the examiner's rejection is not proper.

Withdrawal of the rejection is respectfully requested.

Response to Applicant's Arguments

Applicant's arguments have been carefully considered but not deemed persuasive because the US Pat. Nos. 5,100,663, 4,616,079, 4,699,898, 4,710,380, 4,778,750, 4,874,608, 5,013,546, 5,081,108, 5,093,321 were searched for guidance regarding the terms "Leukocyte Dialysate subfraction" and "Purified Leukocyte Dialysate Subfraction", but such guidance is not sufficient to provide evidence of possession of the full scope. With respect to Leukocyte Dialysate, US 4,619,079 teaches in cols. 1-3 that:

> The present invention relates to the discovery of (1) methods for extracting "amplifiers" of the immunity system, which are isolated from dialyzed extracts of leukocytes and (2) the amplifiers themselves that are so extracted."
>
> "In the cited copending application, eight specific modulators of the human immune system were described that have been isolated from dialysates of leukocyte extracts. Six such modulators described therein have amplifier activity and two have suppressor activity. These six amplifiers were designated amplifiers 1-6. These two suppressors were identified as the S-suppressor and the L-suppressor. "
>
> "Some of the work in this field was summarized and commented on by A. Uotila, in Transfer Factor and Other Immunological Activities of Human Leukocyte Dialysate and Other Dialysates of Mammalian Tissues (1979). Uotila's monograph indicates that preparations of so-called "transfer factor" may contain a large variety of substances. Uotila suggested that an "augmenting activity" can be derived from dialyzable leukocyte extracts in guinea pigs, but did not disclose whether this is one or several different materials or activities, or if the latter, how to separate them from one another. As explained in the specification of the cited copending application, the inventor believes that this monograph is of interest primarily because it teaches away from the disclosure of the copending, and also the instant, patent application."

Therefore, not all leukocyte dialysates have the desired activity (only the fractions that have amplifier propertires, rather than suppressor properties or those fractions of Uotila's monograph containing a large variety of substances, some of them being inactive. Additionally, as evidenced by Applicant's own arguments regarding the 102 (b) rejection over Gottlieb (US 4,468,379), Applicant stated that neither the L-suppressor nor the S-Suppressor have the same activity as the immunomodulator or immunoamplifier fraction (applicants' arguments, page 10, 8/28/2008). The guidance provided as to what a subfraction is of a leukocyte dialysate is not sufficient for one of ordinary skill in the art to know what fraction(s) have the desired activity in a method of controlling chronic inflammation associated with Metabolic Syndrome. Further

examination of the rest of cited prior art patents (5,100,663, 4,699,898, 4,710,380, 4,778,750, 4,874,608, 5,013,546, 5,081,108, 5,093,32) does not shed further light regarding how the instantly claimed purified leukocyted dialysate subfraction with the instantly claimed activity can be obtained by one of ordinary skill in the art and which subfractions do not have the desired activity. Additionally, please note that Applicant's arguments center around the definition of leukocyte dialysate subfraction as being "naturally derived from healthy human leukocytes, as well as purified immunologically active components of the naturally derived immunoregulators including the dipeptide tyrosylglycine (YG) and the tripeptide tyrosylglycylglycine (YGG), as well as synthetically produced YG and YGG", However, the instant claims are already drawn to YG and YGG, therefore the making and using of the purified leukocyte dialysate subfraction, and how it differs from YG and YGG, is not adequately described, after carefully considering all the patents incorporated by reference.

The written description rejection is therefore maintained.

Conclusion

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCELA M. CORDERO GARCIA whose telephone number is (571)272-2939. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cecilia Tsang/
Supervisory Patent Examiner, Art Unit 1654

/Marcela M Cordero Garcia/
Examiner, Art Unit 1654

MMCG 05/09